REMARKS/ARGUMENTS

Claims 1 and 30 remain in the application. Claims 1 and 30 have not been amended. The REMARKS/ARGUMENTS have been rewritten to address shortcomings in the response previously filed on March 27, 2006. Reconsideration of this application, as amended, is respectfully requested.

Claims 1 and 30 stand rejected under 35 U. S. C. §102(e) as being anticipated by Schwartz (U. S. 2003/0013857 A1). This rejection is respectfully traversed for the following reasons.

The present invention provides an improved method for conjugating macromolecules. See paragraph [0014]. The method comprises contacting a First Macromolecule to a reactive support to form a solid-bound macromolecular complex. If necessary, either or both steps of activating the First Macromolecule and deactivating the unreacted reactive moieties on the reactive surface are performed. A Second Macromolecule is activated, if necessary, and contacted to the First Macromolecule. After the solid, First Macromolecule, and Second Macromolecule bind to form a ternary complex, the bond between the solid and the First Macromolecule is disrupted to provide a macromolecular conjugate that is preferably soluble or dispersible in aqueous solution. See paragraphs [0015], [0024], [0025], [0037], [0050], [0055], [0056], [0057].

One or more additional optional steps can be performed to add additional macromolecules and smaller molecules or atoms to the Macromolecular Conjugate. Any additional optional steps are preferably performed prior to disruption of the bond between the solid and the First Macromolecule. See paragraphs [0016], [0037].

Each step of the process, in fact the entire process, is preferably performed under aqueous conditions suitable to maintain the biological activity of an enzyme (e.g., bovine alkaline phosphatase). See paragraphs [0018], [0023].

The Examiner indicated that the Applicant failed to address the issues addressed by the Examiner in the Officer Actions of November 1, 2005 and March 7, 2005. It is true that the Applicant failed to present a persuasive argument for patentability. According, the Remarks/Arguments

herein will show that Schwartz U.S. Patent Application Publication No. 2003/0013857 A1 fails to teach a method comprising all of the steps of the method described and claimed in this application.

Schwartz, U.S. Patent Application Publication No. 2003/0013857 A1 (hereinafter "Schwartz"), discloses modified solid supports that include solid supports that have been modified by reaction with a bifunctional reagent that possess a hydrazine or oxyamino group. These modified solid supports are useful in immobilization of biomolecules that possess or are modified to possess a carbonyl group. In one embodiment, aliphatic bifunctional hydrazide reagents are provided. These reagents include a cleavable bond for further manipulation. Cleavable bonds include, but are not limited to, acid cleavable, photocleavable and disulfide bonds.

In Schwartz, paragraph [0110] describes the use of cleavable linkers to create a drug-antibody conjugate, which is cleaved by physiological processes following endocytosis. Schwartz also refers to the use of cleavable disulfide linkages to isolate receptors following covalent linking between a ligand and a receptor. Paragraph [0111] of Schwartz describes the use of bifunctional hydrazides to modify biomolecules or carriers in a single step. These modified aliphatic hydrazide molecules or carriers can be subsequently reacted with carbonyl containing biomolecules, drug, or other therapeutic or diagnostic reagent to form a hydrazone that can be cleaved following exposure to mild aqueous acid conditions. Paragraph [0112] of Schwartz describes that solid supports such as beads, chromatographic supports or surfaces are modified with aliphatic hydrazide reagents.

Paragraph [0147] of Schwartz describes hydrazino modified beads for forming stable hydrazones when reacted with molecules possessing carbonyl groups. Paragraph [0150] of Schwartz describes hydrazine and oxyamino silanes that are useful for modification of silica surfaces to generate hydrazine and oxyamino glass, including, but limited to controlled pore glass; hydroxyamino and oxyamino slides; and hydrazine and oxyamino silica chips. Paragraph [0158] of Schwartz describes reagents to incorporate hydrazine and oxyamino groups on thiophilic metals, surfaces and particles. Paragraph [0177] of Schwartz describes that the reagent provided therein may be utilized to form crosslinks between a wide variety of molecules, including. for

example, protein-protein conjugates (e.g., monoclonal antibody/enzyme conjugate) or protein-polymer conjugates (e.g., monoclonal antibody to a microtiter well surface). Paragraph [0179] of Schwartz describes immobilization of biomolecules to surfaces using a crosslinking couple by modifying the biomolecule with either a hydrazino, oxyamino, or a carbonyl moiety and contacting the modified biomolecule to a surface possessing its reactive partner, e.g., a hydrazino or oxyamino moiety for a carbonyl-modified biomolecule, or a carbonyl moiety for a hydrazino- or oxyamino-modified biomolecule. EXAMPLE 6 of Schwartz describes modification of glass surfaces by a hydrazone-protected hydrazine silane reagent. EXAMPLE 7 of Schwartz describes preparation of 96 well plates to incorporate aromatic aldehyde moieties. EXAMPLE 8 of Schwartz describes preparation of 96 well plates to incorporate aromatic hydrazine moieties. EXAMPLE 18 of Schwartz describes a general procedure for the modification of gold particles with succinimidyl hydrazinium modification reagent. EXAMPLE 21 of Schwartz describes immobilization of horseradish peroxidase to hydrazine-modified plates.

Schwartz provides a number of descriptions of conjugations between biomolecules and solid supports. Schwartz also provides a number of descriptions of cleavable linkers. However, Schwartz does not disclose or suggest a method for carrying out the methods described in claims 1 and 30 of this application. For example, claims 1 and 30 of this application describe the preparation of a conjugate in which (1) a first macromolecule is linked to a solid surface through a disruptable linker (see, for example, paragraphs [0035] and [0036] of this application), (2) a second macromolecule is linked to the first macromolecule, and (3) the linker between the solid surface and the first macromolecule is disrupted, thereby (4) releasing the conjugate comprising the first macromolecule that is linked to the second macromolecule.

Upon a review of Schwartz, it can be seen that Schwartz describes methods for attaching a first macromolecule to a second macromolecule. See for example, paragraphs [0110], [0111], and [0112] of Schwartz. Schwartz also describes methods for attaching a chain of macromolecules to a surface. See, for example, paragraphs [0147], [0150], [0158], [0177], [0179], and

EXAMPLES 6, 7, 8, 18, and 21 of Schwartz. However, Schwartz fails to disclose or suggest a multiple-step method that includes the steps of (1) linking a first macromolecules to a surface, (2) linking a second macromolecule to the first macromolecule, and (3) disrupting the link between the first macromolecule and the surface in order to free the conjugate comprising the first macromolecule and the second macromolecule from the surface. Accordingly, Schwartz does not disclose a method containing all of the steps of the method described and claimed in this application. For this reason, it is submitted that Schwartz does not anticipate claims 1 and 30 of the present application.

In view of the foregoing, it is submitted that claims 1 and 30 are in condition for allowance, and official Notice of Allowance is respectfully requested.

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Respectfully submitted,
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